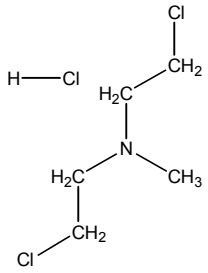
NITROGEN MUSTARD HYDROCHLORIDE
CAS No. 55-86-7
First Listed in the *Fourth Annual Report on Carcinogens*



CARCINOGENICITY

Nitrogen mustard hydrochloride is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC S.4, 1982; IARC S.7, 1987; IARC V.9, 1975). The generic name nitrogen mustard is used interchangeably with nitrogen mustard hydrochloride, and since only nitrogen mustard hydrochloride is produced, it was assumed to be nitrogen mustard hydrochloride under study. When administered topically, nitrogen mustard hydrochloride induced local papillomas and squamous cell carcinomas in female mice. When administered by intravenous injection, it induced tumors in different organs in rats. When administered by subcutaneous, intravenous, or intraperitoneal injection, the compound induced lung tumors and lymphomas in mice.

An IARC Working Group reported that there was limited evidence for the carcinogenicity of nitrogen mustard hydrochloride in humans (IARC S.7, 1987). Case reports and epidemiological studies of humans exposed to nitrogen mustard hydrochloride alone were not available to IARC Working Groups, except for one study involving the treatment of mycosis fungoides. In this study, squamous cell carcinomas occurred after long-term topical therapy with nitrogen mustard hydrochloride for mycosis fungoides. Treatment with the compound in combination with other cytotoxic drugs and/or radiation resulted in many cases of leukemia and various malignant tumors in patients with Hodgkin's disease and other solid tumors (IARC S.4, 1982).

PROPERTIES

Nitrogen mustard, in its pure form, occurs as a dark liquid with a faint fishy odor. It is fairly volatile and decomposes slowly on standing, forming the polymeric quaternary ammonium salt. It is very slightly soluble in water. Nitrogen mustard hydrochloride, which is the form produced commercially for sale, is composed of large white, hygroscopic crystals that are soluble in water and methanol. When heated to decomposition, nitrogen mustard hydrochloride emits very toxic fumes of hydrochloric acid and other chlorinated compounds as well as nitrogen oxides (NO_x). Dry crystals are stable up to 40°C. Aqueous solutions of nitrogen mustard hydrochloride are not stable. Solutions in DMSO, 95% ethanol or acetone are stable for 24 hours under normal laboratory conditions. Initial pH of a 2% aqueous solution is 3.0-4.0 (Radian, 1991).

USE

Currently, the only known commercial use of nitrogen mustard is as a chemical intermediate in the production of its hydrochloride (IARC V.9, 1975). Nitrogen mustard hydrochloride is used as an antineoplastic agent, either alone or in combination with other chemotherapeutic agents, to treat neoplastic diseases, including Hodgkin's disease, leukemia, generalized lymphosarcoma, mycosis, fungoides, and bronchogenic carcinoma. Also, it is used to control pleural, peritoneal, and pericardial effusions caused by metastatic tumors. Clinical investigations have been performed in the past to evaluate its usefulness in treatment of rheumatoid arthritis, in tissue transplantation studies, and a variety of other nonmalignant diseases. Research has also been conducted to investigate its use as a chemosterilant and as a cross linking agent for the manufacture of ion-exchange fibers. Formerly, the pure form of nitrogen mustard was produced for use as a vesicant in chemical warfare (IARC V.9, 1975).

PRODUCTION

One U.S. company has produced an unreported amount of nitrogen mustard hydrochloride since 1950. The substance is not listed in the 1979 TSCA Inventory. In 1974, 3.3 lb of nitrogen mustard hydrochloride were manufactured and sold in the United States. The pure form of nitrogen mustard is not produced commercially (IARC V.9, 1975).

EXPOSURE

The primary routes of potential human exposure to nitrogen mustard hydrochloride are injection, inhalation, and dermal contact. For patients receiving the chemical as a chemotherapeutic agent, it is administered by intravenous injection in a single total dose of 0.4 mg/kg body weight or in 2 or 4 daily doses of 0.1-0.2 mg/kg body weight (IARC V.9, 1975). The National Occupational Exposure Survey (1981-1983) indicated that 4,618 total workers, including 2,398 women, potentially were exposed to the compound in the workplace (NIOSH, 1984). Potential occupational exposure may occur for health professionals (e.g., pharmacists, nurses, and physicians) involved in cancer chemotherapy during drug preparation, administration, or cleanup. However, the risks can be reduced through use of appropriate containment equipment and work practices (Zimmerman et al., 1981). Potential occupational exposure may occur during the captive production of nitrogen mustard, and the manufacture, formulation, and packaging of nitrogen mustard hydrochloride pharmaceuticals. Nitrogen mustard hydrochloride is not known to occur in nature (IARC V.9, 1975).

REGULATIONS

EPA regulates nitrogen mustard hydrochloride under the Superfund Amendments and Reauthorization Act (SARA), subjecting it to reporting requirements. EPA has proposed regulating nitrogen mustard as a hazardous constituent of waste under the Resource Conservation and Recovery Act (RCRA). FDA regulates nitrogen mustard hydrochloride under the Food, Drug, and Cosmetic Act (FD&CA) as a prescription drug approved for human use. Under FD&CA, nitrogen mustard hydrochloride must have warning labels regarding potential carcinogenicity, mutagenicity, teratogenicity, and/or impairment of fertility. OSHA regulates nitrogen mustard under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-97.